

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau(43) International Publication Date
12 September 2003 (12.09.2003)

PCT

(10) International Publication Number
WO 03/073981 A3(51) International Patent Classification⁷: **A61K 39/395**(21) International Application Number: **PCT/SE03/00347**(22) International Filing Date: **4 March 2003 (04.03.2003)**(25) Filing Language: **English**(26) Publication Language: **English**(30) Priority Data:
0200667-4 5 March 2002 (05.03.2002) SE
10/092,919 8 March 2002 (08.03.2002) US(71) Applicant (for all designated States except US): **ORTHOPAEDIC RESEARCH & DEVELOPMENT IN GOTHENBURG AB [SE/SE]; Gustavsg 35, S-431 66 Mölndal (SE).**

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(75) Inventor/Applicant (for US only): **OLMARKER, Kjell [SE/SE]; Gustavsgatan 35, S-431 66 Mölndal (SE).**(74) Agent: **AWAPATENT AB; Box 5117, S-200 71 Malmö (SE).**(81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.(84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).**Published:**

— with international search report

(88) Date of publication of the international search report:
27 November 2003*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*(54) Title: **NOVEL OF CYTOKINE INHIBITORS**

(57) Abstract: The use of substance that inhibits a pro-inflammatory cytokine, such as TNF or IL-1, for the production of a pharmaceutical composition for improving wound healing is disclosed. Also a method for improving wound healing wherein a therapeutically effective amount of a substance that inhibits a pro-inflammatory cytokine is administered to a patient in need of said treatment is disclosed.

**WO 03/073981 A3**

A. CLASSIFICATION OF SUBJECT MATTER

IPC7: A61K 39/395

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC7: A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

SE,DK,FI,NO classes as above

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	STN International, File ZCAPLUS, accession no. 2002:199887, document no. 136:323691, Kaser, Arthur et al, "Infliximab in severe steroid-refractory ulcerative colitis: A pilot study", & Wiener Klinische Wochenschrift (2001), 113(23-24), 930-933 --	1-24
X	STN International, File MEDLINE, accession no. 2000046083, document no. 20046083, Heller T. et al, "Treatment of severe esophageal Crohn's disease with infliximab", & INFLAMMATORY BOWEL DISEASES, (1999 Nov) 5 (4) 279-82 --	1-24

☒ Further documents are listed in the continuation of Box C.☐ See patent family annex.

* Special categories of cited documents:

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier application or patent but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
- "&" document member of the same patent family

Date of the actual completion of the international search

18 June 2003

Date of mailing of the international search report

23-06-2003

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C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	STN International, File MEDLINE, accession no. 2001011857, document no. 20409486, Jojic N., "[Pharmacotherapy of inflammatory bowel disease]. "Farmakoterapija inflamatornih bolesti creva", & ACTA CHIRURGICA JUGOSLAVICA, (2000) 47 (1-2) 51-5 --	1-24
X	STN International, File MEDLINE, accession no. 2001419273, document no. 21360250, Blam M.E., "Integrating anti-tumor necrosis factor therapy in inflammatory bowel disease: current and future perspectives", AMERICAN JOURNAL OF GASTROENTEROLOGY, (2001 Jul) 96 (7) 1977-97 --	1-24
X	STN International, File MEDLINE, accession no. 2001553668, document no. 21486185, Travis S.P. et al, "Treatment of intestinal Behcet's syndrome with chimeric tumour necrosis factor alpha antibody", & GUT, (2001 Nov) 49 (5) 725-8 -- -----	1-24

INTERNATIONAL SEARCH REPORT

International application No.
PCT/03/00347**Box I** Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: **25-48**
because they relate to subject matter not required to be searched by this Authority, namely:
A method for treatment of the human or animal body by therapy,
see rule 39.1
2. ☒ Claims Nos.: **1-24**
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
see next sheet
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

Present claims 1-24 relate to a substance defined by reference to a desirable characteristic or property, namely that inhibits a pro-inflammatory cytokine for treatment of a wound by improving wound healing. The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and / or disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lacks clarity (Article 6 PCT). An attempt is made to define the compound by reference to a result to be achieved. Further, the wording "a substance that inhibits a pro-inflammatory cytokine" and similar expressions in the claims are not clear and concise. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has mainly been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely the use of the example compound infliximab for the production of a pharmaceutical composition for treatment of a wound by improving wound healing.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established will not be the subject of an international preliminary examination (Rule 66.1 (e) PCT). This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.